REMARKS

Introduction

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow. This amendment is a supplemental amendment to the previous Amendment and Reply filed January 9, 2009. Applicant renews the arguments presented in the previous response.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims, claims 2, 8, 34, 35, 37, and 45-48 are pending. Claim 49 is requested to be canceled without prejudice or disclaimer. Solely in the interest of advancing prosecution, claims 34 and 48 are currently being amended. Support for the new and amended claims can be found throughout Applicant's specification, no new matter was added. Applicant reserves the right to pursue the original claims and/or claim of greater or lesser scope in related applications.

Applicant respectfully requests reconsideration and further examination of the subject application in light of the foregoing amendments and the following remarks.

Interview summary

The following constitutes a statement of the substance of the interview as required under MPEP §713.04.

On Thursday, February 26, 2009 Examiner Shay conducted a telephone interview with Applicants' attorneys John Garvey (the undersigned) and Matthew Fenselau, along with inventor Eric Bornstein. Applicants discussed the claims in view of the prior art of record. No agreement on the claims was reached. However, the participants agreed on amendments to the claims which Examiner Shay indicated would likely, subject to more careful analysis on his part, distinguish the prior art of record.

Prior Art of Record

Neuman

In the interview, the participants discussed Neuman (Biophysical Journal, Vol. 77, November 1999). Applicants noted that Neuman is directed to optical tweezers which are near infrared based optical traps (created for cell biology), which use infrared laser beams to hold and study single cells of various prokaryotic and eukaryotic species while keeping them alive and functional under a microscope.

The Examiner noted that Neuman does discuss damage caused to bacterial by trapping beams having wavelengths which fall within Applicants' claimed ranges. However, Applicants pointed out that Neuman fails to teach or suggest a control system which controls "photodamage bacteria at the infected site without detrimental heat deposition or irreversible harm to the biological system at the infected site."

To the contrary, Neuman studied the effects of his laser trapping beams on both prokaryotic bacterial cells(*E. Coli*) and eukaryotic mammalian cells (CHO) at the power densities

appropriate for optical trapping. He found "rough similarity between the wavelength dependence of photodamage" seen in the two types of cells (Neuman, page 2861, columns 1-2). This finding led Neuman to deduce that there was likely a "common basis for damage" in both types of cells. (Neuman, page 2861, column 2). Neuman therefore warned that "the region of the spectrum between 870 and 910 nm is particularly damaging and should be avoided, ***especially for work in vivo***."(Neuman, page 2862, second column, emphasis added). [1] This is because, based on his findings regarding, Neuman concluded that these wavelengths would damage **not only bacterial cells, but also surrounding tissue.**

Accordingly, Applicants argued that a person skilled in the art would recognize that Neuman teaches away from the use of the claimed wavelengths in applications where one seeks to photodamage bacteria without causing harm to the surrounding biological system (e.g. *in vivo* applications).

Applicants noted that, in contrast, while it is to be understood that the scope of the claims is not limited to the specific examples found in the specification, Applicants' disclosure describes a discovery that, at suitable power densities, the claimed wavelengths may be employed to selectively photodamage bacteria without harming the surrounding system:

> Instead of avoiding the 870 nm and 930 nm wavelengths as suggested in the prior art by optical tweezer procedures, the laser system and process of the present invention selectively combines them. With less heat deposition in the site being irradiated, a much enlarged therapeutic window of opportunity is available to the laser operator. In essence, the combined wavelengths of the present invention use less energy than do prior art procedures to effect bacterial destruction, i.e. the optical energy used in the present invention is less than the thermal energy used in the prior art. (Applicants specification, paragraph 0051).

A person skilled in the art would not have expected this result based on the teachings of Neuman. Rather, Neuman explicitly taught that wavelengths in these ranges would indiscriminately damage **both** (prokaryotic) bacterial cells and the (eukaryotic) cells of surrounding biological

[1] See also Figs. 5 and 6 of Neumann. Note that in Fig. 6 the action spectrum for photodamage the E. Coli and CHO cells are shown in terms of LD_{50} and cloning efficiency respectively such that the *minima* in the graph correspond to *maximum* photodamage.

system.

Applicants further noted that there is enabling support for the above mentioned limitation throughout Applicants' specification, e.g. a paragraphs 0011, 0044, 0051 (quoted above), 0058, and 0062. The above passages describe an exemplary techniques for determining suitable dosages (e.g. power densities and treatment times) for a given application. For example, one may apply light in the claimed ranges and proceed by "maintaining exposure until a desired change is observed or cultured."(paragraph 0058). The passages cited above also disclose how power density my be suitably adjusted to photodamage bacterial without detrimental heat deposition or irreversible harm to the biological system at the infected site:

> It is adjustable by increasing power (always below tissue coagulation potential), by increasing spot size, or by scanning the tissue with a set spot of high intensity and minimal size. The mortality ratio is directly proportional to power density increase. It is not necessary to kill all bacteria. It is necessary only to kill sufficient bacterial to enable the body's immune system to clear the rest.

Paragraph 0011 provides substantial guidance as to avoidance detrimental heat deposition or irreversible harm to the biological system:

> Normal human temperature is 37° C, which corresponds to rapid bacterial growth in most bacterial infections. When radiant energy is applied to a biological system with a near infrared diode laser, the temperature of the irradiated area starts to rise immediately, with each 10° C. rise carrying an injurious biological interaction. At 45° C. there is tissue hyperthermia, at 50° C. there is a reduction in enzyme activity and cell immobility, at 60° C. there is denaturation of proteins and collagen with beginning coagulation, at 80° C. there is a permeabilization of cell membranes, and at 100° C. there is vaporization of water and biological matter. In the event of any significant duration of a temperature above 80° C (five to ten seconds in a local area), irreversible harm to the biological system will result.

Based on this information, a person skilled in the art would easily be able to tailor applied dosages (i.e. power density, exposure time, etc.) to avoid detrimental heat deposition or irreversible harm to the biological system.

The above passages constitute considerable direction and guidance in practicing the

invention. Applicant further notes that the field of medical laser devices is highly developed, and that one or ordinary skill in the art would have clearly understood the materials and methods needed to practice the invention, at the time the application was filed, in view of the large body of available technical literature and the teachings of the application. Thus, based on the above guidance, a person skilled in the art could have, without undue experimentation, made and used a control for a laser oscillator which effected bacterial photodamage without detrimental heat deposition or irreversible harm. See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, Applicants' disclosure would have allowed a person skilled in the art to "make and use the claimed invention," as required to satisfy 35 U.S.C. §112. M.P.E.P. §2164.

In view of the above, Applicants respectfully submit that sole independent claim 34 patentably distinguishes Neuman, either alone and in combination with the other prior art of record.

L'Esperance

In the interview, the participants discussed L'Esperance (U.S. Patent No. 4,951,663). Applicants noted that L'Esperance is directed to a photosterilization system, and explicitly teaches the microbial ingestion of a photosensitizer which "enables selective destruction of microorganisms in reaction to penetrating laser irradiation." (Column 2, lines 15-17.) This photosensitizer acts as an **exogenous** chromophore in the microorganisms for absorption of the laser irradiation. (L'Esperance, column 5 line 57 through column 6 line 23). Applicant further notes that use of such a chromophore would be inappropriate for the present invention, since the chromophore would also be taken up by host cells, thereby sensitizing them as well to the laser treatment. Notably, the methods of L'Esperance would not permit therapeutic application of laser energy to the infected site "*without detrimental heat deposition or irreversible harm to the biological system at the infected site*", which is required by claim 34.

In contrast, Applicant's invention seeks to exploit properties of the infectious agents

rather than simply causing local sterilization by thermal means to both host and microbial cells that have been sensitized by an exogenous chromophore, as taught by L'Esperance. Solely in the interest of advancing prosecution, Applicants have amended independent claim 34 to recite "*selective emission of near infrared energy at the power density from the laser oscillator system for absorption by* ***endogenous*** *bacterial chromophores*." Support for this amendment may be found at paragraph 0088 of Applicants' specification.

In view of this, Applicants respectfully submit that claim 34, as amended patentably distinguishes L'Esperance either alone and in combination with other prior art of record.

L'Esperance and Neuman

Applicants further submit that a person skilled in the art would not have combined the L'Esperance and Neuman to result in Applicant's . As discussed in detail above, Neuman explicitly teaches away from the use of the claimed wavelengths for *in vivo* applications, because his studies indicated that laser radiation at those wavelengths would damaged **both** bacterial cells and the cells of the surrounding biological system. The purpose of the L'Esperance device is the "**selective** destruction of microorganisms" (column 2, lines 15-17) and explicitly teaches that, for *in-vivo* treatment, damage (including "photon optical damage") of the surrounding living tissue should be avoided (column 1 lines 58-68). Accordingly, a person skilled in the art would have avoided the use of the claimed wavelengths in the device of L'Esperance, because Neuman teaches that such wavelengths cause indiscriminate damage of **both** bacterial and surrounding tissues.

Accordingly, Applicants submit that there is no proper basis for the combination of L'Esperance and Neuman. The Office Action, appears to agree with this position.

35 USC § 112 Rejections

Claim 43 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 43 has been cancelled, thereby obviating this issue.

35 USC § 103 Rejections

Claims 34, 37, and 43

In the Office Action, the Examiner rejected claims 34, 37, and 43 under 35 U.S.C. § 103(a) as being unpatentable over international application WO 2000/01294 to Parker at al. ("Parker") in combination with U.S. Patent No. 5,295,143 to Rao ("Rao"). Applicant traverses the rejection and requests reconsideration in view of the claims as amended and for the following reasons.

For a rejection under 35 U.S.C. § 103(a), the cited reference(s) must teach or suggest each and every limitation in the claim(s) at issue. A further requirement necessary for a rejection under 35 U.S.C. § 103(a) is that it would have been obvious to one skilled in the art combine or modify the reference(s) in the way proposed by the Examiner. Both requirements are not met in this situation, and Applicant therefore respectfully traverses the rejection and requests reconsideration.

Claim 34, the sole remaining independent claim, recites a laser system for therapeutic treatment of bacteria in an infected site, the system comprising:

> (a) a laser oscillator system configured and arranged to selectively emit near infrared radiation at a power density in one or both of a first wavelength range of about 865 nm to about 875 nm and a second wavelength range of about 925 nm to about 935 nm;
>
> (b) a control connected to the laser oscillator system, the control configured and arranged to control the selective emission of near infrared energy at the power density from the laser oscillator system for absorption by endogenous bacterial chromophores as non-ionizing optical energy to photodamage bacteria at the infected site without detrimental heat deposition or irreversible harm to the biological system at the infected site;

(c) an optical channel connected to the laser oscillator system, the optical channel configured and arranged for transmission of the near infrared radiation; and

(d) a head configured and arranged to deliver the near infrared energy from the laser oscillator system and the optical channel to bacteria in the infected site at the power density for absorption at the infected site. (Emphasis added).

Parker does not teach or suggest such a system. To the contrary, Parker is directed to and teaches the use of a blood constituent monitor including a light transmitter and a plurality of optical fibers positioned to direct light to a body and a light detector for detecting light transmitted through or reflected from the body. See, e.g., Parker, page 5, lines 19-25 and claim 1. The detected transmitted or reflect light is analyzed to determine information about blood constituents.

There is no teaching whatsoever in Parker to apply near-infrared energy for absorption, where laser system comprises a control system that allows application of the laser at a power density that will photodamage bacteria at the infected site without detrimental heat deposition or irreversible harm to the biological system at the infected site. Absorption of laser energy by the Parker device, rather than reflection or transmission of the light applied to the body as taught by Parker, would render the Parker device incapable of its intended purpose as an analytic tool for blood sugar monitoring.

Further, Parker does not teach or suggest selectively emitting near infrared radiation at a power density in one or both of a first wavelength range of about 865 nm to about 875 nm and a second wavelength range of about 925 nm to about 935 nm. The Office Action, (page 3) alleges that Parker teaches "applying multiple wavelengths to the body by separate channels at numerous wavelengths in each of applicant's claimed ranges." Applicant respectfully disagrees with this characterization of Parker.

It appears a point of confusion has arisen between the light applied to the body by the Parker device and the subsequent detection and spectral analysis of reflected or transmitted light. Applicant draws the Examiner's attention to the fact that Parker describes using *in vivo* testing that utilizes a broadband light source consisting of a 400W quartz-halogen light source. Light from the broadband source is directed to the body. A portion of light reflected from or transmitted through the body is detected by a multi-channel photodiode (MCPD) spectrophotometer to generate spectrally resolved test data. The test data is analyzed by software supplied with the MCPD spectrophotometer to "access data points at 1.94nm intervals with the wavelength range 300-1100 nm." (See Parker, page 9, lines 1-11.)

While Parker mentions several wavelength ranges which appear to be similar to those found in Applicant's claims, these ranges are not related to applied treatment light of any sort. Instead, the ranges are discussed in the context of analyzing spectrally resolved test data generated by the detection of reflected/transmitted light:

> The analysis which is presented here uses the same wavelength range used in the previous glucose studies carried out namely: 805nm, 925nm, 970nm and the broadband average 1000-1100nm, but additionally wavelength sampled at regular intervals in the entire range 800nm to 1100nm. Intervals of 1.96nm worked well. (Page 8, lines 10-14, Emphasis added).

Thus Parker makes it clear that it is the spectrophotometer software that provides the ability to utilize the data at the "regular intervals" and not that light is supplied in discrete wavelengths exactly at these intervals:

> Using the supplied software, the instrument allows access to data points at 1.94nm intervals within the wavelength range 300-100nm. The range displayed during the glucose experiments was 500-1100nm. (Page 9, lines 5-9)

Thus one skilled in the art would understand that Parker teaches "sampling" of specific optical data at regular intervals across a broad spectrum but not actual application of such wavelengths at such intervals.

In view of the above, Applicant submits that Parker et al. does not teach or suggest the application of laser energy at near infrared wavelength ranges as claimed by the Applicant in the subject application. Moreover, Parker et al. does not appreciate or recognize the advantages of applying near infrared wavelength ranges to bacteria. In fact there is not a single aspect of Parker et al. that teaches or suggests using his device on bacteria in an infected site, or using light to photodamage bacteria. Parker et al. simply uses a light source and a detector to measure metabolic products of humans in human blood. The device would not be sufficient to cause bacterial photodamage through, for example, creation of reactive oxygen species.

Rao does not cure the deficiencies of Parker. Initially, Applicant submits that a person skilled in the art would not have combined Rao and Parker as proposed by the Office Action. The Office Action alleges that:

> Rao et al teach the production of a wavelength range encompassing the entirety of applicant's wavelength range with a titanium sapphire laser. It would have been obvious to the artisan of ordinary skill to employ the laser of Rao et al in the device of Parker et al, since this would produce the desired wavelengths at precisely controllable wavelength, power, and intensity values, thereby enabling more accurate measurement, thus producing a device such as claimed.

Applicant respectfully disagrees. As noted above, Parker teaches a medical diagnostic tool which directs broadband light to a portion of a patient's body, detects light reflected or transmitted therefrom, and performs spectral analysis on the detected light to determine blood constituent levels (e.g. glucose levels). There is no indication in Parker that a light source featuring precisely controllable wavelength, power, and intensity values would provide improved results, or would be any way desirable for this application. To the contrary, the use of a titanium sapphire laser light source would add unnecessary cost and complexity, likely rendering the Parker device unsuitable for its intended purpose. Parker teaches the use of a cheap, simple

broad band halogen lamp light source. A titanium sapphire laser is many orders of magnitudes more expensive, much larger, requires specialized safety measures, and is so complex as to require substantial expertise for use and maintenance.

A person skilled in the art therefore would recognize that such a complicated source is simply inappropriate for use in a relatively simple medical diagnostic device. For example, a device featuring a titanium sapphire laser would be completely unsuited for use as a home blood glucose meter, as envisioned by Parker. (See Parker, page 4, lines 20-24). Thus, a person skilled in the art would not have combined Parker and Rao as proposed in the Office Action. Accordingly, the proposed combination does not provide proper basis for the rejection under 35 USC § 103(a).

Further, even assuming, *arguendo*, that that the proposed combination of Parker and Rao were proper, it would still fail to teach or suggest each and every element of Applicant's claim. The Office cites Rao as teaching "production of a wavelength range encompassing the entirety of Applicant's wavelength range with a titanium sapphire laser." Applicant points out that Rao is directed to a three color laser for printing that can produce colors in the visible spectrum of light. Rao does not teach therapeutic application of near infrared radiation to a bacterial locale.

Rao generates near IR frequencies, but these frequencies are then modulated to produce light with a blue spectrum. See, col. 2, lines 23-30. The 850-950nm spectra generated by Rao is simply an initial way to generate coherent light that is then frequency shifted to a desired range of 425-475nm, which is then utilized as a blue beam for printing. Rao actually teaches away from Applicant's claimed invention, as the nonvisible frequencies generated by the laser are not used themselves, but need to be frequency doubled to achieve a visible frequency. Light in this visible frequency range is not suitable for absorption as non-ionizing optical energy without detrimental heat deposition or irreversible harm to the biological system at the infected site to photodamage bacteria at the infected site.

Rao does not envision or discuss application of near infrared laser energy to humans. In fact, Applicant notes that laser printers commonly have significant warning labels advising users to avoid beam exposure. Similarly, the device of Rao does not indicate it can be used to damage bacteria in an infected site. There is nothing in that reference that teaches or suggests using near infrared lasers to create photodamage to bacteria, or to use such lasers on a person or at a site of infection.

Thus, the combination of Parker and Rao, even if proper, does not teach (and seems to teach away from) each and every limitation recited in the claims, and therefore these references are an improper basis for a rejection of the claims under 35 U.S.C. § 103(a).

Claims 37 and 43 depend from claim 34, and thus are patentable for at least the same reasons.

Claims 35 and 44

Claims 35 and 44 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Parker in combination with Rao, both previously discussed, in further view of U.S. Patent No. 6,377,828 to Chaiken ("Chaiken"). Applicant traverses the rejection and requests reconsideration for the following reasons.

The Examiner cites Chaiken as teaching use of a power of at least 100 mW for performing non-invasive measurements. Without acceding to what Chaiken actually teaches or the propriety of the motivation alleged for the rejection, Applicant submits that Chaiken fails to remedy the shortcomings of Parker and Rao relative to independent claim 34. Accordingly, the rejection of claims 35 and 44 is improper and should be removed.

Claims 2 and 8

In the Office Action, the Examiner rejected claims 2 and 8 under 35 U.S.C. § 103(a) as being unpatentable over Parker and Rao, both discussed previously, in further view of Rosenthal

(U.S. Patent No. 6,968,221). Applicant traverses the rejection and requests reconsideration for the following reasons.

The Examiner cites Rosenthal as teaching the use of two optical channels in a finger clip. Without acceding to what Rosenthal actually teaches, or the propriety of the motivation alleged for the rejection, Applicant submits that Rosenthal fails to remedy the shortcomings of Parker and Rao relative to independent claim 34. Accordingly, the rejection of claims 2 and 8 is improper and should be removed.

Response to Applicant's Previous Arguments

In response to arguments presented in a previous response, the Office Action (page 2) alleges that Applicant's claimed wavelength ranges are not critical, as they do not produce an unexpected result. Applicant respectfully disagrees. Applicant notes that MPEP § 716.02 and MPEP § 2144.05(III) set forth established law holding that unexpected results arising from the criticality of a claimed subrange can provide for patentability of claims reciting the subrange. Such a claimed subrange can be patentable over any prior art which teaches broad ranges without comprehension of the uniqueness or unexpected results arising from the claimed subrange.

As Applicant has stated in the subject application, the claimed near infrared wavelengths range of Applicant's invention are capable of treating bacteria in an infected site by causing photodamage with non-ionizing optical energy and minimal heat deposition (e.g. sufficiently small to avoid thermolysis or bacterial or surrounding tissue). (See, e.g., paragraphs 13 and 99 of the subject application.) The prior art of record teaches the application of an enormously broad spectrum of wavelengths for a variety of purposes, very little of which could be used to produce the bacterial photodamage claimed by Applicant. These references fail to comprehend the uniqueness of the Applicant's claimed near infrared wavelengths and ranges, and do not teach or suggest the use of such specific and narrow wavelength ranges for producing photodamage in bacteria in an infected site while avoiding unwanted heating and/or irreparable damage to the surrounding biological system.

New Claims

New claims 45-49 depend from independent claim 34, and thus are patentable for at least the same reason.

Support for claims 45 and 46 can be found at, e.g., paragraphs 48 and 92 of Applicant's specification. Support for claim 47 can be found at, e.g., paragraph 99 of Applicant's specification. Support for claims 48-49 can be found at, e.g., paragraphs 44 and 62 of Applicant's specification.

Double Patenting

In the Office Action, the Examiner issued provisional rejections of claims of the subject application, including remaining claims 34, 35 and 37, over five of the Applicant's co-pending applications: 11/825,550; 11/841,348; 11/981,486; 11/997,665; and, 12/019,336.

Applicant respectfully requests that these provisional rejections be held in abeyance until such time that all other rejections in the subject application have been resolved.

Conclusion

In view of the above, Applicant respectfully submits that there is no proper basis for the rejections under 35 USC § 112 and 35 USC §103. Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application. Applicant intends to contact the Examiner shortly after the filing of this document to request an interview to discuss the subject application and related application bearing Serial No. 10/649,910.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date March 11, 2009

By _____

John M. Garvey
Attorney for Applicant
Registration No. 37,833

FOLEY & LARDNER LLP
Customer Number: 48329
Telephone: (617) 342-4085
Facsimile: (617) 342-4001